WHAT IS CLAIMED IS:

1. A method for producing a cloned ungulate wherein the expression of both copies of a gene essential for B cell production has been knocked out, selected from the group consisting of Igα, E2A, EBF, BSAP, rag-1 and rag-2, which comprises the following steps:

(i) producing a male and/or female ungulate cell wherein the expression of one or both copies of the Igα, E2A, EBF, BSAP, rag-1 and/or rag-2 gene has been eliminated by targeted disruption;

(ii) using said cell or DNA therefrom as a donor for nuclear transfer by fusing or inserting said donor cell or nucleus into an oocyte or blastomere, which is enucleated before or after transfer, activating the resulting nuclear transfer unit and/or the oocyte prior or simultaneous to nuclear transfer and culturing in a suitable medium to produce a nuclear transfer embryo;

(iii) introducing said nuclear transfer embryo into a female ungulate; and

(iv) obtaining a cloned fetus or animal ungulate that expresses the genotype of the donor differentiated cell, in which one or both copies of the, Igα, E2A, EBF, BSAP, rag-1 and/or rag-2 gene have been eliminated: and

(v) optionally, mating said cloned male or female ungulate with another cloned female ungulate wherein one copy of the rag-1 or rag-2 gene has been knocked out and selecting progeny wherein both copies of the Igα, E2A, EBF, BSAP, rag-1 or rag-2 genes have been knocked out.

2. The method of claim 1, wherein the expression of both copies of the E2A, Igα, EBR, BSAP, rag-1 and/or rag-2 gene is eliminated, by a three-step process comprising the following steps:

(i) a desired ungulate cell is contacted with a DNA construct that provides for targeted deletion or inactivation of said Igα, E2A, EBF, BSAP, rag-1 or rag-2 gene by homologous recombination;

(ii) the resulting differentiated cell or DNA therefrom, wherein the expression of one copy of the Igα, EBF, E2R, BSAP, rag-1 and/or rag-2 gene has been knocked out, is used as a nuclear transfer donor and is fused or inserted into an enucleated oocyte;

(iii) the resulting nuclear transfer unit is allowed to develop into an embryo, and a cell is obtained from this embryo and is contacted with a second DNA construct under conditions that results in the elimination of the expression of the other (second) copy of the Igα, E2A, EBF, BSAP, rag-1 and/or rag-2 gene; by homologous recombination; and

(iv) the resulting cell, in which both copies of the Igα, E2A, EBF, BSAP rag-1 and/or rag-2 gene have been knocked out, is used as a nuclear donor for nuclear transfer by fusing or inserting said donor cell or DNA therefrom into an enucleated oocyte or blastomere, activating the resultant nuclear transfer unit after oocyte prior to nuclear transfer, and culturing in a suitable medium to produce a nuclear transfer embryo which does not express E2A, EBF, BSAP, Igα, rag-1 or rag-2.

3. The method of claim 1, wherein the ungulate cell used for homologous recombination is a differentiated cell derived from ectoderm, mesoderm or endoderm.

4. The method of claim 1, wherein the donor differentiated cell is a ibroblast cell.

5. The method of claim 1, wherein the cloned ungulate is selected from the group consisting of bovines, pigs, horses, sheep, buffalo and goats.

6. The method of claim 1, wherein the differentiated cell of (i) is produced by sequentially contacting said cell with two knockout constructs which in combination provide for knockout of both copies of the Igα, E2A, EBF, BSAP, rag-1 and/or rag-2 genes.

7. The method of claim 6, wherein the said two knockout constructs comprise different selectable markers thereby providing for the selection of cells wherein both copies of the rag-1 and/or rag-2 are eliminated.

8. The method of claim 1, wherein said method further comprises the step of introducing the double knockout embryo of (iv) into a female ungulate in order to produce a fetus or live offspring.

9. The method of claim 8, wherein the hematopoietic stem cells are introduced into said cloned fetus while *in utero* or said live offspring shortly before or after birth.

10. The method of claim 9, wherein the human hematopoietic stem cells are introduced into said cloned ungulate within about 48 hours to one week before or after birth.

11. The method of claim 9, wherein said hematopoietic stem cells become stably engrafted and result in the formation of functional human B and T lymphocytes.

12. The method of claim 11, wherein human B and T lymphocytes are isolated from the cloned ungulate.

13. The method of claim 11, wherein said human B cells produce human immunoglobulins.

14. The method of claim 11, wherein human immunoglobulins are isolated from the cloned ungulate.

15. A transgenic ungulate wherein both copies of the rag-1 and/or rag-2 gene have been knocked out.

16. The transgenic ungulate according to claim 15 which is selected from the group consisting of bovine, pig, sheep, goat, horse and buffalo.

17. The transgenic ungulate of claim 16 which is a bovine.

18. The transgenic bovine of claim 17 which comprises stably engrafted hematopoietic stem cells of a different species than bovine.

19. The transgenic bovine of claim 18 which comprises human hematopoietic stem cells.

20. The transgenic bovine of claim 18 which comprises canine, feline, murine or primate hematopoietic stem cells.

21. A method of making non-bovine antibodies from a bovine completely isolating antibodies from the serum of a transgenic bovine according to claim 18.

22. The method of claim 21 wherein said antibodies are human.

23. A method of producing hybridomas comprising:

(1) obtaining B cells from a transgenic bovine according to claim 18;

(2) fusing said cells with an immortal cell to produce a hybridoma cell line.

24. The method of claim 23 wherein said B cells are human B cells.

25. The method of claim 23 wherein said transgenic bovine is immunized with a desired antigen prior to isolation of B cells treatment.

26. The method of claim 25 wherein said B cells are human.

27. A method of expanding human B cells comprising engrafting human hematopoietic stem cells into a transgenic ungulate according to claim 15; and allowing said human hematopoietic stem cell to become stably engrafted and expand in said transgenic ungulate.

28. The method of claim 27 which further comprises recovering said human B and T cells from said transgenic ungulate.

29. A method for maintaining desired tissues, organs or cells in vivo comprising:

(i) engrafting desired allogeneic or xenogeneic tissues in a transgenic ungulate according to claim 15; and

(ii) incubating said tissue in said animal.

30. The method of claim 29 wherein said tissue comprises skin, heart, lung, pancreatic, liver or kidney tissue, cells or organs.